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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/415,795	ZHOU ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36,39,41-43,46-49 and 57-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36, 39, 41-43, 46-49 and 57-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 7, 2004 has been entered.

The amendment filed April 7, 2004 canceling claims 12, 13, 16-35, 44, 45 and 50-56, amending claims 36, 39, 41-43 and 47 and adding claims 57-70 has been entered.

Claims 36, 39, 41-43, 46-49 and 57-70 are pending.

Specification

The disclosure is objected to because it describes "βTrCP" as "a human homolog of Cdc4p" (pages 11 and 138, for example). As explained in Applicants' Remarks of April 7, 2004 (page 11, 1st paragraph), this is incorrect.

Correction is required.

Claim Objections

Claims 36, 39, 41-43, 46-49, 62, 65-67, 69 and 70 are objected to reciting non-elected inventions SEQ ID NOs:2, 6, 8, 10 and 12 encoded by SEQ ID NOs:1, 5, 7, 9 and 11, respectively.

Applicants elected SEQ ID NO:4 that is encoded by SEQ ID NO:3 (Response filed May 29, 2001, Office action mailed October 3, 2003).

Claims 36, 39, 41-43, 46-49, 62, 65-67, 69 and 70 have only been examined with respect to the elected invention of SEQ ID NO:4.

Claim 41 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 41 is dependent from claim 36. Claim 36 recites six F-box polypeptides whereas claim 41 recites eight F-box polypeptides.

Claim 42 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 42 is dependent from claim 36. Claim 36 recites "an F-box consisting of an amino acid sequence" whereas claim 42 recites "an F-box comprising an amino acid sequence". As

"comprising" is an open language and "consisting of" is a closed language, claim 42 has a broader scope than claim 36.

Applicant is advised that should claim 57 be found allowable, claim 58 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim 57 recites "F-box comprises amino acids 148-192 of SEQ ID NO: 4" and claim 58 recites "F-box consisting essentially of amino acids 148-192 of SEQ ID NO: 4". "Comprising" and "consisting essentially of" are both the open language transitional phrases that mean the same, i.e. both require the entire contiguous sequence of amino acids 148-192 of SEQ ID NO: 4 without substitutions, insertions, or deletions (although the open claim language permits additional sequences before and/or after the recited sequence).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 36, 39, 41-43, 46-49, 60, 62 and 63 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 36 has been amended to recite "a nucleotide sequence that is at least 90% identical to the nucleotide sequence in SEQ ID NO:3 that encodes amino acids 148-192 of SEQ ID NO:4". Claim 42 has been amended to recite "a nucleotide sequence that is at least 95% identical to the nucleotide sequence in SEQ ID NO:3 that encodes amino acids 148-192 of SEQ ID NO:4". Claim 60 recites "a nucleotide sequence that is at least 95% identical to a nucleotide sequence of SEQ ID NO:3 encoding a WD domain in SEQ ID NO:4".

While the specification provides support for a nucleotide sequence that is at least 90% or 95% identical to a "nucleic acid sequence of a sequence shown in one of the sequence listings" (page 20, last paragraph, emphasis added), the examiner is unable to locate adequate support in the specification for at least 90% or 95% identity to a fragment of a specific nucleotides sequence, including SEQ ID NO:3. Furthermore, there is no support for a nucleotide sequence that is at least 90% or 95% identical to any nucleotide sequence that is not listed in the Sequence listing. This includes no support for a nucleotide sequence encoding a specific amino acid sequence of SEQ ID NO:4 other than a nucleotide sequence of SEQ ID NO:3. With regard to claim 60, the examiner is unable to find support for a chimeric sequence comprising F-box encoded

by a fragment of SEQ ID NO:3 (i.e.100% identical) and further comprising a WD domain encoded by a nucleotide sequence that is at least 95% identical to SEQ ID NO:3 Thus there is no indication that above sequences were within the scope of the invention as conceived by Applicants at the time the application was filed.

Claims not specifically discussed herein are rejected as dependent from the rejected base claim.

Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

Claims 36, 39, 41-43, 46-49 and 57-64 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 36, 39, 41-43, 46-49 and 57-70 recite a genus of hybrid polypeptides comprising F-box and a target interaction domain wherein the F-box recruits the hybrid polypeptide to a Skp1/Cul1/F-box protein (SCF).

Claim 36 recites "F-box consisting of an amino acid sequence that is encoded by a nucleotide sequence that is at least 90% identical to the nucleotide sequence in SEQ ID NO:3 that encodes amino acids 148-192 of SEQ ID NO:4". Claim 42 recites "F-box [that] comprises an amino acid sequence that is encoded by a nucleotide sequence that is at least 95% identical to the nucleotide sequence in SEQ ID NO:3 that encodes

amino acids 148-192 of SEQ ID NO:4". Claims 36, 39, 41, 43, 46-49 and 57-64 depend thereon. Thus, the claims do not identify the structure of the claimed F-box in terms of its length and sequence.

Therefore, many structurally and functionally unrelated F-box polypeptides are encompassed within the scope of these claims. The specification discloses a method of use of only two species of F-box containing polypeptides, *Saccharomyces cerevisiae* Cdc4 (SEQ ID NO:2) and human βTrCP (SEQ ID NO:4) (SEQ ID NO:4 is 13.2% identical to SEQ ID NO:2). Two representative species are insufficient to describe the entire highly variable genus of F-box polypeptides that recruit the hybrid polypeptide of any structure to a Skp1/Cul1/F-box protein (SCF) composed of undefined sequences. The specification fails to describe any other representative species by any identifying characteristics or properties other than being an F-box polypeptide and fails to provide any structure: function correlation present in all members of the claimed genus.

Further, the genus of "target polypeptide interaction domain" recited in claims 36, 39, 41-43, 46-49 and 57-70 encompasses polypeptides of greatly variable structure and function. The specification discloses only two species of the genus of target interaction domain, LTP and E7N, resulting in three species of a hybrid polypeptide, a hybrid of Cdc4 with LTP and E7N and a hybrid of βTrCP fused with E7N. In these cases, a known interaction domain was fused to a known component of a known ubiquitin pathway and used for degrading a respective target. The specification fails to describe any other representative species by any identifying characteristics or properties other

than being a target polypeptide interaction domain and any structural information commonly possessed by members of the genus which distinguish the protein species within the genus from other proteins such that one can visualize or recognize the identity of the members of the genus.

Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 36, 39, 41-43, 46-49 and 57-70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for targeting a target polypeptides using hybrid polypeptides comprising an F-box of Cdc4 or βTrCP and known target polypeptide interaction domain, such as LTP and E7N, in yeast and human cells, respectively, does not reasonably provide enablement for a method of use of a hybrid polypeptide comprising any F-box and any target polypeptide interaction domain for targeting for ubiquitin proteolysis in any eukaryotic cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of

direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Factors pertinent to this discussion include predictability of the art, guidance in the specification, breadth of claims, and the amount of experimentation that would be necessary to use the invention.

Claims 36, 39, 41-43, 46-49 and 57-70 are drawn to a method of use of any hybrid polypeptide comprising any F-box and a target polypeptide interaction domain in any eukaryotic host cell "wherein the F-box recruits the hybrid polypeptide to a Skp1/Cul1/F-box protein (SCF) ubiquitin ligase complex". In *S. cerevisiae*, SCF comprises Skp1/Cdc53 and F-box protein, Cdc4. In a human cell, SCF ubiquitin ligase complex comprises human homologs of Skp1/Cdc53 and F-box protein, βTrCP. The SCF ubiquitin ligase complexes are multimeric complexes that comprise other components.

The art teaches that "F-box proteins directly contact ubiquitination substrates and can display selectivity in recognition of potential targets for ubiquitination, as would be expected of E3 proteins" (Skowyra et al., form PTO-1449 mailed November 14, 2000, reference AF, page 215, 2nd column). The art teaches the composition of *S. cerevisiae* SCF ubiquitin ligase complex (*ibid*, for example).

However, the composition of SCF ubiquitin ligase complexes and ubiquitin proteolysis pathways are not yet elucidated in most eukaryotic cells and for most

targets. The art teaches that substitution of Cdc4 by another *S. cerevisiae* F-box protein Grr1 did not "support ubiquitination of phosphorylated Sic1 complexes" (Skowyra et al., *supra*, page 213, 2nd column). Without knowing the composition of a SCF ubiquitin ligase complex including its F-box protein and its target, it is impossible to construct a requisite hybrid. Without knowing the pathway it is impossible to reconstitute it *in vitro*.

The specification teaches a method of use of a hybrid of Cdc4 with LTP and E7N for degrading pRB when both the hybrid and pRB were expressed in *S. cerevisiae* Y81 cells (page 135). The specification further teaches a method of use of a hybrid of a human F-box protein, βTrCP, fused with E7N for degrading the endogenous protein, p107, that is human pRB analog, when expressed in human C33A cells (pages 138-139, Figure 11, page 140). Therefore, the specification teaches a method of use of a F-box polypeptide, Cdc4, for targeting a known target polypeptide in *S. cerevisiae* and a method of use of human F-box protein, βTrCP, fused to a known target polypeptide interaction domain, for degrading of a known target polypeptide in human cells.

The specification does not support the broad scope of the claims because of the following.

Thus, the specification teaches the use of Cdc4/βTrCP based hybrids in a host cell naturally containing other components of a SCF ubiquitin ligase complex. The hybrid is cell specific, i.e., Cdc4 is used in yeast cells and βTrCP is used in human cells. The specification provides no guidance or working examples as to how to use the claimed method in other eukaryotic cells. The specification does not teach how to use a

hybrid comprising E7 and LTP and a second component other than Cdc4 in cells containing no pRB or p107.

In addition, with regard to claim 39, the specification does not teach what renders the proteolysis not proteosome mediated and how to distinguish among various mechanisms.

Therefore, one of ordinary skill in the art would require guidance, in order to degrade any target polypeptide by using a hybrid comprising any F-box other than a hybrid based on Cdc4 and βTrCP and known target polypeptide interaction domain in *S. cerevisiae* and human host cell, respectively, in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

Claims 65-70 are further rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a hybrid protein comprising F-box of SEQ ID NO: 4, does not reasonably provide enablement for a hybrid protein comprising F-box polypeptide encoded by a nucleotide sequence that is at least 90% identical to SEQ ID NO:3 or by a nucleotide sequence that hybridizes to SEQ ID NO:3 under medium stringent hybridization conditions comprising 0.2 x SSC at 50° C and recruits the hybrid polypeptide to an SCF ubiquitin ligase complex of any structure. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The scope of the claim is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of F-box polypeptides broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and amino acid sequence of a single F-box polypeptide having the amino acid sequence of SEQ ID NO: 4.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claim which encompasses any F-box polypeptide encoded by a nucleotide sequence that is at least 90% identical to SEQ ID NO:3 or a nucleotide sequence that hybridizes to SEQ ID NO:3

under medium stringent hybridization conditions comprising 0.2 x SSC at 50° C because the specification does **not** establish: (a) regions of the protein structure which may be modified without effecting F-box activity; (B) the general tolerance of F-box polypeptide to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any F-box polypeptide residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any F-box polypeptide encoded by a nucleotide sequence that is at least 90% identical to SEQ ID NO: 3 or a nucleotide sequence that hybridizes to SEQ ID NO:3 under medium hybridization conditions comprising 0.2 x SSC at 50° C. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of F-box polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36, 39, 41-43, 46-49 and 57-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 36 recites a hybrid polypeptide comprising "F-box", "wherein the F-box recruits the hybrid polypeptide to a Skp1/Cul 1/F-box protein (SCF)". It is unclear whether the same sequences are encompassed by the term "F-box" in both instances. It is further unclear which sequences other than the sequences of *S. cerevisiae* Skp1/Cdc53 and their human homologs are encompassed by the terms "Skp1/Cul 1". Claim 36 recites "F-box in SEQ ID NOs: 2, 6, 8, 10 or 12". Claim 43 that depends from claim 36 recites "F-box in any of SEQ ID NOs: 2, 4, 6, 8, 10 and 12". The specification defines F-box in SEQ ID NO:4 as residues 148-192 (page 30) but does not define it in other sequences. Claim 36 recites "a nucleotide sequence that is at least 90% identical to the nucleotide sequence in SEQ ID NO:3 that encodes amino acids 148-192 of SEQ ID NO:4". The claim is confusing because it is unclear which sequences are intended to be claimed, the 135 nucleotides of SEQ ID NO:3 that encode residues 148-192 or any fragment of SEQ ID NO:3 that comprises said 135 nucleotide fragment, including the full length sequence of SEQ ID NO:3. Depending on the length of the fragment the percent identity will vary resulting in the different scope of the encoded F-box peptides. Similarly unclear is claim 42.

Claim 39 appears to be missing words in "proteolysis is by the proteasome".

Claim 41 recites "an F-box polypeptide selected from the group consisting of Cdc4p, Pop1p, Pop 2p, Grr1p, Met30p, HOSp, beta TrCP, and FWD1". It is unclear

which sequences other than SEQ ID NOs; 2, 4, 6, 8,10 and 12 are encompassed by the terms Cdc4p, beta TrCP, Grr1p, Met30p, Pop 2p, and FWD1, respectively. It is unclear which polypeptides are encompassed by the terms Pop1p and HOSp. Further, it is unclear why some polypeptides end with "p" while others such as "beta TrCP, and FWD1" are not.

Claim 49 recites "the target polypeptide is selected from the group consisting of a retinoblastoma polypeptide, a p107 polypeptide, IkB, Sic1p, Cln2p, E2 or beta-catenin". It is unclear which polypeptide sequences are encompassed by the recited terms.

Claims 65 and 790 recite "an SCF ubiquitin ligase complex". It is unclear which sequences compose said complex.

Claims not specifically discussed herein are rejected as dependent on the rejected base claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 36, 39, 41-43, 46, 47, 49, 65-67, 69 and 70 are rejected under 35 U.S.C. 102(a) as being anticipated by Kumar et al.

Kumar et al. (PNAS (March 1998), 95, 2417-2422) teach that "F-boxes operate independently of WD-repeats " (page 2417, 2nd column). They teach chimeric

polypeptides wherein F-box of SCON2 proteins were replaced with foreign F-box containing proteins such as Cdc4p and Met30p expressed in fungus *Neurospora*. Kumar et al. teach that "the ability of these swapped domains to at least partially function within SCON2 suggests a common underlying mechanism of action, possibly involving F-box-mediated proteolysis. Regardless of the underlying mechanism, Kumar et al. teach a method of targeting a polypeptide comprising F-box and a target interaction domain for proteolysis in a eukaryotic cell.

Response to Arguments

Applicant's arguments filed April 7, 2004 have been fully considered but they are not persuasive.

With regard to the 112, 1st paragraph, written description rejection, Applicants argue that "Skp1 proteins are highly conserved from one eukaryotic species to another (see, e.g., Fig. IC of Bai et al., (1996) Cell 86:263, attached hereto as Exhibit B). Thus, F-boxes are highly conserved from one protein to another within the same species and across species. This is shown, e.g., in Fig. 3 of Patton et al., *supra*, which shows an alignment of the F-box of 38 proteins from *S. cerevisiae* and Fig.4A of Bai et al., *supra*, showing the homology of F-boxes across the species' (Remarks, paragraph bridging pages 8-9). This is not persuasive because the claims do not require the presence of specific conserved residues in F-box peptide but claim F-box peptide by its ability to bind to Skp1/Cul1. The structural limitations in claim 36 are unclear, *supra*. F-box peptide claimed by both a clear structural definition and its function 9ability to bind to

Skp1/Cdc53, for example) would be sufficiently described. Further, Applicants argue Thus, since the claimed hybrid proteins have a common structure due to the presence of the F-box, a person of skill in the art would recognize that the inventors had possession of the invention at the time of filing. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested " (page 9, last paragraph). this is not persuasive because it is not a common structure that is claimed but a great number of structures having an unknown identity.

With regard to the 112, 1st paragraph, enablement rejection, Applicants argue that "The specification further describes that target polypeptide interaction domains, if not known, can readily be isolated (see, e.g., pages 33 to 58) " (page 10). This is not persuasive because while the claims are enabled for the use of a hybrid protein comprising 148-192 fragment of SEQ ID NO:4 or a highly homologous protein that binds to human homologs of Skp1/Cdc53 in a human cell, are not enabled for use of any F-box with any target interaction domain in any eukaryotic cell. There is no use for targeting of a polypeptide that is not known.

Applicants further refer to the post filing articles to support their arguments (page 11). It is noted that these articles (Zhang et al., Liu et al., Su et al., Cong et al.) all describe the use of βTrCP fusion proteins in human cells and cannot support the claim for any eukaryotic cell for the reasons discussed above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

July 9, 2004